IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
DALLAS DIVISION

AMNIOTIC THERAPIES, LLC Plaintiff, v. U.S. FOOD AND DRUG ADMINISTRATION, Defendant.	)	Case No. 3:16-cv-2412

MEMORANDUM IN SUPPORT OF EMERGENCY MOTION FOR TEMPORARY RESTRAINING ORDER

Plaintiff Amniotic Therapies, LLC ("Amniotic Therapies") files this Memorandum in Support of its Motion for Temporary Restraining Order to stay the effectiveness of an Order issued by the United States Food and Drug Administration ("FDA") two days ago. The FDA Order, which was delivered to Amniotic Therapies late in the afternoon Tuesday, August 16, would compel Amniotic Therapies to stop manufacturing and distributing all but a handful of its amniotic tissue-based wound products, to recall all those products it has distributed, and to destroy all those products. Under the FDA Order, which – absent action by this Court – takes effect in five working days (that is, at 3:10 p.m. Tuesday, August 23, 2016), Amniotic Therapies would also not be able to resume manufacturing and distributing the relevant products until FDA determines that it will permit Amniotic Therapies to do so. The FDA Order would have predictably devastating consequences for Amniotic Therapies, and there is no reason for the Order to take immediate effect, since the Order is based on an FDA inspection that took place three and one half months ago, ending on May 4, 2016.

For reasons explained more fully below, the Order is also unfounded, and was issued in violation of the Administrative Procedure Act ("APA"), 5 U.S.C. §§ 551-583, 701-706, which prohibits agencies like FDA from engaging in actions that are arbitrary and capricious, an abuse of discretion, or otherwise not in accordance with law. First, no defects have been found in any of the products that FDA is ordering Amniotic Therapies to recall, destroy, and halt production of. Second, the conditions that FDA found objectionable have all been corrected or remediated, and FDA has been informed of the corrections. Third, FDA is permitted, under the applicable statute, to take such dramatic enforcement action only upon a finding that the products present a "source of dangerous infection to human beings." Here, the only "infection to human beings" that has been identified by FDA occurred after administration of *different* products to patients, and, critically and demonstrably, likely because of errors in surgical practice by the operating surgeon, not because of the products themselves.

Accordingly, Amniotic Therapies meets the standards required for issuance of a Temporary Restraining Order and Preliminary Injunction. The Court should stay the effectiveness of the FDA Order until it has the opportunity to determine whether final relief is appropriate.

FACTS

The FDA Order at issue here, attached to the Appendix in Support of Motion for Temporary Restraining Order as Exhibit 4 (App. 13-18) was delivered to Amniotic Therapies at 3:10 p.m. on Tuesday, August 16, 2016. The FDA Order states that, after an FDA inspection that concluded on May 4, 2016 (App. 13), FDA found conditions that were in violation of FDA regulations described further below, and that the "conditions of manufacture . . . do not provide adequate protections against the risks of communicable disease transmission" because of those regulatory violations, and that there are "reasonable grounds to believe" that the relevant

products "pose a danger to health" (*id.*). The Order stated that it did not apply to three products manufactured by Amniotic Therapies: AlphaGEMS, AlphaGEMS Nano, and AlphaGEMS Micro (*id.* at n.1). As to products other than those in the AlphaGEMS family, the Order (App. 14) requires Amniotic Therapies to cease distributing the products, to issue a recall for them, and to destroy them, within five working days. The Order, which included information about Amniotic Therapies' right to request a hearing (App. 18), did not include any further information about why the perceived failure to comply with regulations created the risks required by statute in order for such an Order to issue.

Amniotic Therapies is registered (under 21 CFR 1271.21 and following) with FDA to process, package, store, label, and distribute amniotic tissue-based wound products. One of the products, AlphaGEMS, is described in its package insert as a "wound covering derived from human amnion," tissue recovered from human placenta (App. 3). The package insert also stresses that the vial containing AlphaGEMS should not be introduced into the sterile field by surgeons, instructing personnel to "open the foil pouch" containing the product "outside the sterile field," and adding that the physician should withdraw the "allograft" (the technical name for the contents of the vial to be administered to a patient) into a "sterile syringe" (App 4). To be clear, these instructions clearly explain to a practicing surgeon that the contents of the vial should be drawn from the vial using a sterile syringe, and that the sterile syringe should be introduced into the sterile field, not the vial itself.

As noted above, this group of AlphaGEMS products is not covered by the FDA Order. Amniotic Therapies also processes and distributes amniotic tissue based wound products for other purposes. The AlphaGEMS product discussed above is a liquid, contained in a vial. The AlphaPATCH product, described in its package insert at App. 60-61, is, consistent with its name,

a solid product that is packaged in a pouch, with similar instructions as to introduction into the sterile field (only the inner pouch, which has been terminally sterilized, may be introduced into the sterile field).

Amniotic Tissues has received only four complaints about use of its products in patients since distribution began in September 2014 (Declaration of Jason Reneau, Paragraph 7 (hereinafter "Reneau Decl."), App. 6). All four were reports from St. Vincent's Hospital in Cleveland, Ohio. The surgeon who used the products on these four patients did not sterilize the vials before bringing them into the sterile field, or withdraw the contents into a sterile syringe and bring only the pre-loaded sterile syringe into the sterile field. The surgeon confirmed these reports to personnel from Amniotic Therapies (Reneau Decl. at Paragraph 8, App. 6; Declaration of Neil Riordan, Paragraph 3 (hereinafter "Riordan Decl."), App. 12).

FDA conducted an inspection at Amniotic Therapies in 2015, and a second inspection on certain dates from early March through early May, 2016 (App. 13). At the end of the 2016 inspection, FDA issued a Form 483, its standard method of reporting inspectional observations (App. 13). Amniotic Therapies responded to the 483 promising corrective actions to address the observations (App. 16). Amniotic Therapies also stated that it would not resume production of amniotic tissue products until the corrective actions were in place.

The FDA 483 (Report of Inspection) reported that its findings were based, in part, on MedWatch reports that had been filed with FDA about the four patients discussed above, and on tests that were conducted on AlphaGEMS vials, reportedly unused, that were in the possession of St. Vincent's Hospital (App. 28-29). During the inspection, Amniotic Therapies repeatedly asked the FDA inspectors for copies of the MedWatch reports, and for copies of shipping documentation relating to the vials from St. Vincent's, which were reportedly tested at the

University of Alabama in Birmingham ("UAB") (Reneau Decl. at Paragraph 13, App. 8). Amniotic Therapies also requested copies of the testing methodology and any documentation describing the testing facilities (*id*). FDA inspectors refused to provide this documentation, which was essential so that Amniotic Therapies could determine the validity of the test results and the conditions under which patients were reported to have suffered adverse events. In conversations subsequent to the inspection, Amniotic Therapies or its lawyer, Mr. Farquhar, repeated its requests for this information. App. 24-25. The government informed Mr. Farquhar that FOIA requests would need to be filed with both FDA and the Centers for Disease Control and Prevention (CDC) to get the information. Those requests were filed (App. 26-31). The FDA documents were received by Amniotic Therapies in virtually illegible form (App. 32-59) and only on the same day that the FDA Order was delivered. The requests for information about the UAB tests, directed to the CDC (as Mr. Farquhar was instructed), have not been addressed.

On August 16, as noted above, the FDA Order was received at 3:10 p.m.

Before filing this motion, Amniotic Therapies notified FDA that it would seek a Temporary Restraining Order in this court. The notification was submitted by email early the morning of August 18, 2016 (at 1:03 a.m., Eastern Standard Time), and resulted in a telephone conversation between lawyers for FDA and for Amniotic Therapies. Amniotic Therapies has agreed to provide copies of these filings to FDA forthwith, and will coordinate with FDA and the Court on scheduling.

Along with the FDA Order, Amniotic Therapies received a Warning Letter, attached at App. 19-23, relating only to the AlphaGEMS family of products. The Warning Letter is an indication that FDA believes that the conditions found at a facility are violative, but is not, in

itself, an enforcement action against the company. Amniotic Therapies has 15 working days to respond to the Warning Letter.

STATUTORY AND REGULATORY BACKGROUND

The production and distribution of amniotic tissue-based wound products, such as those produced by Amniotic Therapies, are regulated under the Public Health Service Act, codified at 42 U.S.C. § 264 which authorizes the Surgeon General of the United States to enforce regulations that permit the destruction of "articles" which are "found to be so infected or contaminated as to be sources of dangerous infection to human beings." The Surgeon General has delegated his authority to promulgate such regulations to FDA.

Regulations issued by FDA pursuant to this statutory provision are included in 21 C.F.R. Part 1271. In relevant part, 21 C.F.R. §1271.400 permits FDA to inspect facilities like Amniotic Therapies, which manufacture amniotic tissue-based wound products. The regulations at 21 C.F.R. §1271.440(a)(1) also provide that FDA may serve upon the person "a written order" that a human tissue product "be recalled and/or destroyed" upon a finding that an establishment is in violation of the regulations in this part," regulations that require manufacturers of such tissue products to follow current good tissue practices, among other requirements.

The APA (5 U.S.C. § 706(2)(A)) directs a reviewing court to "hold unlawful and set aside agency action, findings and conclusions found to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law."

LEGAL ARGUMENT

Under Rule 56 of the Federal Rules of Civil Procedure, the Court has the power to grant a Temporary Restraining Order and Preliminary Injunction when appropriate. In determining whether to issue a TRO, the Fifth Circuit has set out the following four factors: (1) substantial likelihood of success on the merits; (2) a substantial threat of immediate and irreparable harm for

which it has no adequate remedy at law; (3) that greater injury will result in denying the temporary restraining order than from its being granted; and (4) that a temporary restraining order will not disserve the public interest. *Clark v. Princhard*, 812 F.2d 991, 993 (5th Cir. 1987); *Canal Auth. v. Callaway*, 489 F.2d 567, 572 (5th Cir. 1974) (en banc). The party seeking the TRO must satisfy a cumulative burden of proving each of the four elements enumerated before a temporary restraining order can be granted. *See Miss. Power & Light Co. v. United Gas Pipeline*, 760 F.2d 618, 621 (5th Cir. 1985).

A. Amniotic Therapies Is Likely to Succeed on the Merits

The FDA Order falls far short of the requirements necessary to issue an order that would require a regulated processor of human tissue to halt production, to recall products, and to destroy products.

Preliminarily, this matter is ripe for review by the Court. The FDA Order constitutes final agency action, since, even if Amniotic Therapies were to file a request for an administrative hearing, the request for the hearing would only stay the requirement to destroy relevant product, but Amniotic Therapies would still be unable to manufacture (or distribute, as defined in the FDA Order) and would still be required to recall all products, with all the punishing consequences of doing so.

Secondly, the relevant statute does not authorize the FDA to issue a cease and desist/recall order simply because a facility is believed to have violated regulations. Rather, the statute allows issuance of a destruction order only when the articles in question are "…found to be so infected or contaminated as to be sources of dangerous infection to human beings…" (42 U.S.C. § 264), circumstances that are not present here. FDA will likely assert (although it did not do so in the Order) that a threat has been established by the infection of one or more patients at St. Vincent's Hospital who were treated using one of Amniotic Therapies AlphaGEMS

products. Importantly, the product line associated with those events – AlphaGEMS -- is *not* the subject of FDA's Order and is specifically excluded from operation of that Order (App. 13). Rather, that product line is the subject of a separate regulatory process triggered by a Warning Letter issued by FDA on the same day as the Order, which does not require immediate removal of the products from the marketplace or destruction of the products, and affords Amniotic Therapies fifteen days to respond to FDA's allegations contained in the Warning Letter. In light of this contradictory treatment of products produced in the same facility, FDA cannot provide a reasonable basis for asserting that Amniotic Therapies' other product lines pose a substantial threat, warranting immediate recall and destruction, due to the conditions of their manufacture.

Moreover, even if the products that are the subject of the Order had been associated with the Adverse Reactions described above, the patients who may have been exposed to the microbes specified in the MedWatch Reports (App. 35-59) were most likely exposed because of risky behavior of the surgeon, not because of contamination in the product. Discussions with the surgeon involved in the submission of the MedWatch reports make clear that the surgeon did not follow product instructions and introduced the vial into the sterile surgical field, although the outside of the vial had not been sterilized. App. 4. It was not likely the product that caused the infections; it was most likely the surgeon's failure to follow instructions that exposed the patients to risk. No other patients or surgeons have reported any problems with any of Amniotic Therapies' products since distribution began almost two years ago. Reneau Decl. Paragraph 7, App. 6.

FDA will likely also argue that tests performed at UAB on other vials of the same lot of product establish that the product was contaminated. However, the validity of those tests is highly questionable. Despite repeated requests by Amniotic Therapies (Reneau Decl. at

Paragraphs 9, 13 (App. 7-8) and its attorney (App. 24-25), FDA deflected requests for information about the handling of the vials prior to the test, and the methodology and location used to conduct the test, to CDC, and CDC has not even responded to the requests for the documentation surrounding the handling of the vials and the conduct of the test. It would be a fundamental injustice to condemn Amniotic Therapies based on evidence that it hasn't been allowed to see, or to question.

All products referenced in the FDA Order are terminally sterilized (AlphaPATCH and AlphaVISION) and are evaluated for bioburden pre-processing. All AlphaGEMS product lots are tested for sterility pre and post processing.

B. Amniotic Therapies Will Suffer Irreparable Harm if the Injunction Is Not Granted

Absent the requested relief, Amniotic Therapies will suffer immediate irreparable harm for which the company has no other adequate remedy. *See Chacon v. Granata*, 515 F.2d 922, 925 (5th Cir. 1975)). The details of this irreparable harm are hardly surprising: Amniotic Therapies is a small company, with only five employees, at least three of whom would likely have to be laid off if the FDA Order is not stayed, and the company's very existence is in peril. Reneau Decl. Paragraphs 20-28, App. 9-11.

C. Interim Injunctive Relief Will Not Harm FDA or Other Parties

Review of an application for a temporary restraining order also requires the Court to consider whether the adverse party will be injured by imposition of an injunction. This factor also favors issuance of the requested relief here. FDA waited a full three and one half months after completing the inspection before issuing a devastating order with immediate effect. Staying the effective date of the FDA Order until the Court may more deliberately consider the adequacy of the Order will not cause FDA any harm.

D. The Public Interest Supports Granting the Temporary Restraining Order.

The temporary restraining order supports ensuring fair treatment by federal agencies that can wield overwhelming power to destroy businesses, without affording them a chance even to see and challenge important documents on which the agency purports to base its decision (here, test results reporting contaminants allegedly found in AlphaGEMS products). More importantly, the public interest is not served by the FDA Order. Amniotic Therapies' products represent no threat to the public health: the only infections reported occurred when the surgeon failed to heed instructions about maintaining the integrity of the sterile field.

CONCLUSION

For the foregoing reasons, the Court should stay the effectiveness of the FDA Order for 14 days, as permitted by the Federal Rule. A bond is inappropriate in this case, due to the small size of the company, the absence of a threat to the public health, and the lack of any injury to FDA as a result of the Temporary Restraining Order that is sought by Amniotic Therapies.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that a copy of this document was forwarded via email to Shoshana Hutchinson and Perham Gorji of the Office of Chief Counsel of the U.S. Food and Drug Administration on August 19, 2016.

/s/ Joe Kendall
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